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L1: Entry 1 of 1 File: USPT Sep 4, 2001

US-PAT-NO: 6284533
DOCUMENT-IDENTIFIER: US 6284533 B1

TITLE: Plasmid-based vaccine for treating atherosclerosis

DATE-ISSUED: September 4, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thomas; Lawrence J.	Boston	MA		

US-CL-CURRENT: 435/320.1; 424/185.1, 514/44, 536/23.1, 536/23.4, 536/23.5

CLAIMS:

What is claimed is:

1. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, which nucleotide sequence includes at least one segment coding for a B cell epitope of cholesteryl ester transfer protein ("CETP") linked in frame with at least one segment coding for a broad range helper T cell epitope, which nucleotide sequence is operably linked to a promoter sequence suitable for directing the transcription of the nucleotide sequence in a mammalian cell.

2. The DNA immunogenic composition according to claim 1, wherein said at least one segment coding for a B cell epitope of CETP encodes a B cell epitope of human CETP and consists of 8-30 consecutive amino acids of SEQ ID NO:4.

3. The DNA immunogenic composition according to claim 1 wherein said B cell epitope comprises a carboxyl terminal region of CETP, involved in neutral lipid binding or neutral lipid transfer activity.

4. The DNA immunogenic composition according to claim 1, wherein the helper T cell epitope comprises a helper T cell epitope obtained from an antigenic peptide selected from the group consisting of tetanus toxoid, diphtheria toxin, pertussis vaccine, Epstein-Barr virus (EBV), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivatives of tuberculin, keyhole limpet hemocyanin, and combinations thereof.

5. The DNA immunogenic composition according to claim 1 wherein the immunogenic polypeptide includes two B cell epitopes of CETP.

6. The DNA immunogenic composition according to claim 1 which includes a DNA segment coding for each of the two B cell epitopes of CETP, in DNA segment coding for the two B cell epitopes of CETP, in tandem.

7. The DNA immunogenic composition according to claim 1 which includes a DNA segment coding for each of the two B cell epitopes of CETP, in DNA segment coding for the two B cell epitopes of CETP, in tandem.

8. The DNA immunogenic composition according to claim 1, wherein said nucleotide sequence coding for an immunogenic polypeptide comprises the amino acid sequence of SEQ_x ID NO: ".

9. The DNA immunogenic composition according to claim 1, wherein said nucleotide sequence coding for an immunogenic polypeptide includes the amino acid sequence of SEQ_x ID NO:".

10. The DNA immunogenic composition according to claim 1, wherein the promoter is a cytomegalovirus immediate early promoter enhancer.

11. A DNA immunogenic composition comprising a nucleotide sequence comprising:

(a) an immediate early promoter enhancer region of cytomegalovirus (CMV), operably linked to

(b) a structural DNA segment encoding an immunogenic polypeptide and comprising:

(i) a DNA segment encoding amino acids 1 through 3" of SEQ_x ID NO: ",

(ii) a DNA segment encoding amino acids 4"1 through 4"6 of SEQ_x ID NO: 4, and

(iii) a DNA segment encoding amino acids 5"1 through 5"6 of SEQ_x ID NO: 4,

which DNA segments (i), (ii) and (iii) are linked in frame.

12. A DNA immunogenic composition comprising a nucleotide sequence comprising:

(a) an immediate early promoter enhancer region of cytomegalovirus (CMV), operably linked to

(b) a structural DNA segment encoding an immunogenic polypeptide and comprising:

(i) a DNA segment encoding amino acids 1 through 3" of SEQ_x ID NO: ",

(ii) a DNA segment encoding amino acids 4"1 through 4"6 of SEQ_x ID NO: 4, and

(iii) a DNA segment encoding amino acids 5"1 through 5"6 of SEQ_x ID NO: 4,

which DNA segments (i), (ii) and (iii) are linked in frame.

13. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, which nucleotide sequence comprises a first segment coding for a broad range human T cell epitope linked in frame with a second segment coding for a first B cell epitope of chlamydial major transmembrane protein (MOMP) having the nucleotide sequence of nucleotides 1" through 111 of SEQ_x ID NO:", and a third segment coding for a second B cell epitope of MOMP having the nucleotide sequence of nucleotides 11" through 1"1" of SEQ_x ID NO:", wherein the nucleotide sequence coding for the immunogenic polypeptide is operably linked to a promoter sequence suitable for directing the transcription of the nucleotide sequence in a mammalian cell.

14. The DNA immunogenic composition according to claim 13 wherein the nucleotide sequence encodes the nucleotide sequence of SEQ_x ID NO:".

15. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, which nucleotide sequence comprises a first segment coding for a broad range human T cell epitope linked in frame with a second segment coding for a first B cell epitope of chlamydial major transmembrane protein

CETP having the nucleotide sequence of nucleotides 1 to 48 through [illegible] of SEQ ID NO:3 and a third segment coding for a second B cell epitope of CETP having the nucleotide sequence of nucleotides [illegible] through 1407 of SEQ ID NO:3, wherein the nucleotide sequence coding for the immunogenic polypeptide is operably linked to a promoter sequence suitable for directing the transcription of the nucleotide sequence in a mammalian cell.

16. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, which nucleotide sequence comprises a first segment coding for a broad range helper T cell epitope linked in-frame with a second segment coding for a first B cell epitope of cholesteryl ester transfer protein (CETP) having the nucleotide sequence of nucleotides 1-48 through [illegible] of SEQ ID NO:3 and a third segment coding for a second B cell epitope of CETP having the nucleotide sequence of nucleotides 1351 through 1407 of SEQ ID NO:3, wherein the nucleotide sequence coding for the immunogenic polypeptide is operably linked to a promoter sequence suitable for directing the transcription of the nucleotide sequence in a mammalian cell.

17. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, said nucleotide sequence being operably linked to a promoter sequence suitable for directing the transcription of said nucleotide sequence in a mammalian cell, said immunogenic polypeptide comprising a B cell epitope portion, wherein said B cell epitope portion comprises at least one B cell epitope of cholesteryl ester transfer protein (CETP), and a broad range helper T cell epitope portion, wherein said broad range helper T cell epitope portion comprises at least one broad range helper T cell epitope.

18. The DNA immunogenic composition according to claim 17, wherein said at least one B cell epitope of CETP consists of 8-40 consecutive amino acids of SEQ ID NO:4.

19. The DNA immunogenic composition according to claim 17, wherein said at least one broad range helper T cell epitope is a broad range helper T cell epitope obtained from an immunogenic peptide selected from the group consisting of tetanus toxoid, diphtheria toxin, pertussis antigen, Bacille Calmette-Guerin (BCG), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivative of tuberculin, and combinations thereof.

20. The DNA immunogenic composition according to claim 17, wherein said immunogenic polypeptide includes two B cell epitopes of CETP.

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L1: Entry 1 of 1 | File: USPT | Jun. 2[illegible], 2[illegible]

US PAT-NO: 6410020
DOCUMENT-IDENTIFIER: US 6410020 B1

TITLE: Modulation of cholesteryl ester transfer protein (CETP) activity

DATE-ISSUED: June 2[illegible], 2[illegible]

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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US CL-CURRENT: 424/185.1; 424/192.1, 424/192.1, 424/193.1, 424/197.11, 424/204.1, 530/300, 530/324, 530/326

CLAIMS:

I claim:

1. An isolated antigenic hybrid peptide comprising a helper T cell epitope portion linked to a B cell epitope portion, wherein said B cell epitope portion comprises six to 24 consecutive amino acids of the carboxyl terminal 24 amino acids of human cholesteryl ester transfer protein (SEQ ID NO:1).

2. The isolated antigenic hybrid peptide according to claim 1 wherein the helper T cell epitope portion is selected from the group consisting of a helper T cell epitope amino acid sequence of tetanus toxoid, diphtheria toxoid, pertussis vaccine, Bacille Calmette-Guerin (BCG), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivative of tuberculin, keyhole limpet hemocyanin, and combinations thereof.

3. The isolated antigenic hybrid peptide according to claim 1, wherein the helper T cell epitope portion comprises a helper T cell epitope from tetanus toxoid or diphtheria toxoid.

4. An isolated antigenic hybrid peptide comprising the amino acid sequence of SEQ ID NO:1.

5. The isolated antigenic hybrid peptide according to claim 4 consisting of the amino acid sequence of SEQ ID NO:1.

6. The isolated antigenic hybrid peptide according to claim 4, wherein said isolated antigenic hybrid peptide is a fusion of SEQ ID NO:1.

7. A vaccine composition comprising an antigenic vaccine hybrid peptide comprising a universal helper T cell epitope linked to a B cell epitope portion comprising six to 24 consecutive amino acids of the carboxyl terminal 24 amino acids of human cholesteryl ester transfer protein (SEQ ID NO:1).

8. The vaccine composition according to claim 7 wherein the helper T cell epitope portion of said antigenic vaccine hybrid peptide is selected from

group consisting of the amino acid sequence of amino acids 830 to 843 of tetanus toxin protein (amino acids 2 to 15 of SEQ ID NO:2) and the amino acid sequence of amino acids 947 to 967 of tetanus toxin protein (SEQ ID NO:3).

9. The vaccine composition according to claim 7 wherein the T cell epitope portion of the antigenic vaccine hybrid peptide is a universal helper T cell epitope selected from the group consisting of T cell epitope amino acid sequences of tetanus toxoid, diphtheria toxoid, pertussis vaccine, Bacille Calmette-Guerin (BCG), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivative of tuberculin, keyhole limpet hemocyanin, and combinations thereof.

10. The vaccine composition according to claim 7 wherein the antigenic vaccine hybrid peptide further comprises an amino terminal cysteine residue.

11. A method of elevating the ratio of circulating High Density Lipoprotein to circulating Low Density Lipoprotein, Very Low Density Lipoprotein, or total cholesterol in a human or other animal comprising administering to the human or animal an antigenic vaccine hybrid peptide comprising a universal helper T cell epitope portion and a B cell epitope portion, wherein said B cell epitope portion comprises six to 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human cholesteryl ester transfer protein (SEQ ID NO:1).

12. The method according to claim 11 wherein the helper T cell epitope portion of the antigenic vaccine hybrid peptide is selected from the group consisting of the amino acid sequence of amino acids 830 to 843 of tetanus toxin protein (amino acids 2 to 15 of SEQ ID NO:2) and the amino acid sequence of amino acids 947 to 967 of tetanus toxin protein (SEQ ID NO: 3).

13. The method according to claim 11 wherein the antigenic vaccine hybrid peptide further comprises an amino terminal cysteine residue.

14. A method of decreasing the level of cholesteryl ester transfer protein activity in a human or other animal comprising administering to the human or animal an antigenic vaccine hybrid peptide comprising a helper T cell epitope portion linked to a B cell epitope portion comprising six to 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human cholesterol ester transfer protein (SEQ ID NO:1).

15. The method according to claim 14 wherein the antigenic vaccine hybrid peptide is administered in an amount sufficient to elicit production in said human or other animal of anti-cholesterol ester transfer protein antibodies.

16. A method of increasing the level of circulating High Density Lipoprotein in a human or other animal comprising administering to the human or animal an antigenic vaccine hybrid peptide comprising a helper T cell epitope portion and a B cell epitope portion, wherein said B cell epitope portion comprises six to 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human cholesterol ester transfer protein (SEQ ID NO:1).

17. The method according to claim 16, wherein the helper T cell epitope portion is selected from the group consisting of universal helper T cell epitope amino acid sequences of tetanus toxoid, diphtheria toxoid, pertussis vaccine, Bacille Calmette-Guerin (BCG), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivative of tuberculin, keyhole limpet hemocyanin, and combinations thereof.

18. A method of treating atherosclerosis in a human or animal comprising administering to the human or animal an antigenic vaccine hybrid peptide comprising a universal helper T cell epitope portion linked to a B cell epitope portion, wherein said B cell epitope portion comprises six to 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human cholesteryl ester transfer protein.

19. The method according to any one of claims 11, 14, 15, and 18, wherein said antigenic vaccine hybrid peptide is a dimer.

20. A method of making an anti-cholesteryl ester transfer protein (CETP vaccine comprising a B cell epitope portion and a helper T cell epitope portion to modulate endogenous CETP activity, comprising:

selecting a B cell epitope portion from a region of CETP involved in neutral lipid binding or neutral lipid transfer activity;

selecting a helper T cell epitope portion consisting of a helper T cell epitope; and

linking said B cell epitope portion and said helper T cell epitope portion to form a single immunogenic moiety.

21. The method according to claim 20 wherein said B cell epitope portion is covalently linked to said helper T cell epitope portion.

22. The method according to claim 21, wherein said B cell epitope portion is covalently linked to said helper T cell epitope portion via a covalent bond selected from the group consisting of peptide bonds and disulfide bonds.

23. The method according to claim 21 wherein said B cell epitope portion is linked to said helper T cell epitope portion via a cross-linker molecule.

24. The method according to claim 21 wherein said B cell epitope portion is linked to said helper T cell epitope portion via a bridge of amino acids.

25. The method according to claim 21 wherein said B cell epitope portion and said helper T cell epitope portion are linked to a common carrier molecule.

26. The method according to claim 21 wherein said B cell epitope portion is linked to said helper T cell epitope portion to form a vaccine peptide and further comprising the step of linking said vaccine peptide to a carrier molecule.

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L1: Entry 1 of 1 File: USPT Apr 25, 2006

US PAT NO: 6750210
DOCUMENT-IDENTIFIER: US 6750210 B1

TITLE: Modulation of cholesteryl ester transfer protein (CETP) activity

DATE-ISSUED: April 25, 2004

INVENTOR INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Thomas; Lawrence J.	Worcester	MA		

US-CL-CURRENT: 424/193.1; 424/145.1; 424/185.1

CLAIMS:

What is claimed is:

1. A method of elevating the ratio of circulating HDL to circulating LDL, VLDL, or total cholesterol in a human or other animal comprising administering to the human or animal a vaccine composition comprising a peptide conjugate comprising a helper T cell epitope portion linked to a B cell epitope portion, wherein said B cell epitope portion comprises a B cell epitope of a CETP of a human or other animal, and said peptide conjugate, when administered to said human or other animal, elicits production of endogenous antibodies that specifically bind endogenous CETP and results in an elevation of the ratio of circulating HDL to circulating LDL, VLDL, or total cholesterol in said human or other animal.

2. A method according to claim 1 wherein said B cell epitope portion comprises between six and 24 consecutive amino acids of the carboxyl terminal 26 amino acids of human CETP (SEQ ID NO:1).

3. The method according to claim 1 wherein the helper T cell epitope portion of the peptide conjugate comprises a T cell epitope selected from the group consisting of the amino acid sequence of amino acids 41 to 55 of tetanus toxin protein (amino acids 947 to 961 of SEQ ID NO:2) and the amino acid sequence of amino acids 947 to 961 of tetanus toxin protein of SEQ ID NO:2.

4. The method according to claim 1 wherein the B cell epitope portion of the peptide conjugate is selected from the group consisting of between six and 24 consecutive amino acids of SEQ ID NO:1.

5. The method according to claim 1 wherein the peptide conjugate portion comprises an amino terminal cysteine residue.

6. A method of [illegible] CETP activity in a human or other animal comprising administering to the human or animal a peptide conjugate comprising a helper T cell epitope portion linked to a B cell epitope portion, wherein said B cell epitope portion comprises a B cell epitope of a CETP of a human or other animal, wherein said peptide conjugate, when administered to said human or animal, elicits

production of said [illegible] that specifically bind endogenous CETP and results in a decrease in the level of said [illegible] endogenous CETP activity in said human or animal.

7. The method according to claim 6 wherein the peptide conjugate is administered in an amount sufficient to elicit production in said human or other animal of anti-CETP antibodies.

8. A method of altering the metabolism of HDL-cholesterol to decrease the development of atherosclerotic lesions in a human or other animal comprising administering to the human or animal a peptide conjugate comprising a helper T cell epitope portion linked to a B cell epitope portion, said helper T cell epitope portion comprising a broad range T cell epitope and said B cell epitope portion comprising a B cell epitope of CETP, wherein said peptide conjugate, when administered to said human or animal, elicits production of endogenous antibodies that specifically bind endogenous CETP and results in a decrease in the development of atherosclerotic lesions in said human or animal compared to a human or animal not receiving such treatment.

9. A method of increasing the level of circulating HDL in a human or other animal comprising administering to the human or animal a peptide conjugate comprising a helper T cell epitope portion and a B cell epitope portion, wherein said B cell epitope portion comprises a B cell epitope of a CETP of a human or other animal, and wherein said peptide conjugate, when administered to said human or animal, elicits production of endogenous antibodies that specifically bind endogenous CETP and results in an increase in the level of circulating HDL in said human or animal.

10. The method according to claim 9, wherein the helper T cell epitope portion comprises a helper T cell epitope derived from an antigenic peptide selected from the group consisting of tetanus toxoid, diphtheria toxoid, pertussis vaccine, Bacille Calmette-Guerin (BCG), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivative of tuberculin, keyhole limpet hemocyanin, and combinations thereof.

11. The method according to claim 9, wherein the B cell epitope portion comprises a carboxyl terminal region of human CETP consisting of between six and 21 consecutive amino acids of SEQ ID NO:1.